

Appendix

Equations and Parameters for Model Simulations

Ca²⁺ Subspace Model
in Zhang et al., Biophys. J. 84(5):2852–2870 (Figs. 2, 5, 8, 10)

Units:

Conductances	pS
Currents	fA
Ca concentrations	μM
Time	ms
Capacitance	fF

Differential Equations (deterministic):

$$C_m \frac{dv}{dt} = -I_{\text{Ca}} - I_{\text{Kv}} - I_{\text{KATP}} - I_{\text{KCa}} - I_{\text{Leak}} \quad (1)$$

$$\frac{dn}{dt} = \frac{n_\infty(v) - n}{\tau_n} \quad (2)$$

$$\frac{dc}{dt} = f_{\text{CYT}} (-\alpha I_{\text{Ca}} - J_{\text{PMCA}} - J_{\text{SERCA}} + J_X) \quad (3)$$

$$\frac{dc_{\text{ER}}}{dt} = f_{\text{ER}} \left(\frac{V_{\text{CYT}}}{V_{\text{ER}}} J_{\text{SERCA}} - J_{\text{RELEASE}} \right) \quad (4)$$

$$\frac{dc_{\text{SS}}}{dt} = f_{\text{SS}} \left(\frac{V_{\text{ER}}}{V_{\text{SS}}} J_{\text{RELEASE}} - \frac{V_{\text{CYT}}}{V_{\text{SS}}} J_X \right) \quad (5)$$

Initial Conditions:

	Fig. 2	Fig. 5	Fig. 8	Fig. 10
V	-69.3	-54.19	-35.49	-21.366
n	6.12e-5	9.123e-4	0.02481	0.14168
c	0.002835	0.03116	0.05836	0.0516
c_{ER}	14.2	217.2	214.8	193.02
c_{SS}	0.0255	0.3783	0.1394	0.1569

Ionic Currents:

$$I_{\text{Ca}} = g_{\text{Ca}} m_\infty(v)(v - v_{\text{Ca}}) \quad (6)$$

$$I_{\text{KCa}} = g_{\text{KCa}} \omega(v - v_{\text{K}}) \quad (7)$$

$$I_{\text{KATP}} = g_{\text{KATP}}(v - v_{\text{K}}) \quad (8)$$

$$I_{\text{Kv}} = g_{\text{K}} n(v - v_{\text{K}}) \quad (9)$$

$$I_{\text{Leak}} = g_{\text{Leak}}(v - v_{\text{Leak}}) \quad (10)$$

where:

$$n_\infty(v) = \frac{1}{1 + \exp((v_n - v)/s_n)} \quad (11)$$

$$m_\infty(v) = \frac{1}{1 + \exp((v_m - v)/s_m)} \quad (12)$$

$$\omega(c_{\text{SS}}) = \frac{c_{\text{SS}}^q}{c_{\text{SS}}^q + K_d^q} \quad (13)$$

Parameters:

(**bold** denotes changes from model in Fig. 8, Goforth et al, J. Gen. Physiol. 120:307–322, 2002, or preceding figure.)

for I_{Kv} :

g_{Kv}	2500
v_{K}	-70
v_n	-15
s_n	5.6
τ_n	10.8

for I_{Ca} :

	Figs. 2, 5, 10	Fig. 8A	Fig. 8B	Fig. 8C
g_{Ca}	1450	1500	1400	1050
v_{Ca}	30	30	30	30
v_m	-13	-13	-13	-13
s_m	8	8	8	8

for I_{KCa} :

g_{KCa}	1200
K_d	0.7
q	8

for I_{Leak} :

g_{Leak}	14
v_{Leak}	-30

for I_{KATP} :

	Fig. 2A	Fig. 2B	Fig. 5	Fig. 8	Fig. 10
g_{KATP}	1000 → 55	1000 → 62	55	42	60

Calcium fluxes: ($\mu\text{M ms}^{-1}$)

$$J_{\text{PMCA}} = k_{\text{PMCA}} c \quad (14)$$

$$J_{\text{SERCA}} = k_{\text{SERCA}} c \quad (15)$$

$$J_{\text{RELEASE}} = p_{\text{ER}} (c_{\text{ER}} - c_{\text{SS}}) \quad (16)$$

$$J_X = p_X (c_{\text{SS}} - c) \quad (17)$$

with rates: (ms^{-1})

	Fig. 2	Fig. 5	Fig. 8	Fig. 10
p_X	0.025	0.025	0.025	0.025
p_{ER}	0.001	0.001	0.001	0.001
k_{PMCA}	0.2	0.18	0.2	0.2
k_{SERCA}	0.2	0.2	0.2	0.2

and buffer parameters*:

f_{CYT}	0.01
f_{ER}	0.005
f_{SS}	0.04

^{*}(dimensionless fraction of calcium that is free in each compartment)

Volume ratios:

$$\frac{V_{ER}}{V_{SS}} = 0.1 \quad (18)$$

$$\frac{V_{CYT}}{V_{SS}} = 2.5 \quad (19)$$

$$\frac{V_{CYT}}{V_{ER}} = 25.0 \quad (20)$$

$$\frac{V_{SS}}{V_{CYT}} = 0.4 \quad (21)$$

Miscellaneous:

Unit Conversion for ICa (converts fA to $\mu\text{M ms}^{-1}$):

$$\alpha = \frac{1}{2FV_{CYT}} = 4.5 \times 10^{-6} \mu\text{M fA}^{-1} \text{ ms}^{-1}$$

Here 2 is the valence of calcium; F is Faraday's constant; and V_{CYT} is the volume of the cytosol.

Capacitance: $C_m = 5300$

Output function to report the free cytosolic Ca^{2+} that would be reported by fura imaging:

$$c_{AVG} = \frac{V_{SS}c_{SS} + V_{CYT}c}{V_{SS} + V_{CYT}}$$

Noise:

For simulations including channel noise (Figs. 8, 10), I_{KATP} is redefined as

$$I_{\text{KATP}} = \bar{g}_{\text{KATP}}s(V - V_K)$$

where s satisfies the stochastic differential equation (SDE):

$$ds = [\alpha(1 - s) - \beta s]dt + \sigma dW$$

(Note: $-\beta$ is erroneously given as $+\beta$ in Eq. 8 of the paper)
and

$$\sigma = \{[\alpha(1 - s) + \beta s] / [\tau N_{\text{KATP}}]\}^{1/2}$$

with parameters $\alpha = 1 \text{ msec}^{-1}$, $\tau = 100 \text{ msec}$, $N_{\text{KATP}} = 500$, and β chosen such that the deterministic steady state,

$$\frac{\alpha}{\alpha + \beta} = 0.14$$

in Fig. 8 and 0.20 in Fig. 10.

Combined with $g_{\text{KATP}} = 300 \text{ pS}$, this makes the mean values of $g_{\text{KATP}} = 42$ or 60 pS , as stated in the table for I_{KATP} above.

Dynamic Clamping (Fig. 10):

Dynamic clamp current, I_{Clamp} , is added to the V equation and defined as follows:

$$I_{\text{Clamp}} = G_{\max}z(V - 100) \quad (22)$$

$$\frac{dz}{dt} = K(z_{\infty}(V) - z) \quad (23)$$

$$z_{\infty}(v) = \frac{1}{1 + \exp((-30 - v)/7.5)} \quad (24)$$

where $G_{\max} = 0.01 \text{ nS}$; $K = 2 \text{ sec}^{-1}$; and current is turned on at $t = 20 \text{ sec}$.